REMARKS

Claims 1, 25-27 and 29-69 are currently pending in the application. Claims 29-31, 37-39, 41, 42 and 49-51 are currently amended. Claims 26, 27, 37-39, 47, 48, 56-59, 67 and 69 have been canceled without prejudice, and Applicants reserve the right to prosecute these claims in this or a related application. New claims 70-76 have been added. Upon entry of the present amendments, claims 1, 25, 29-36, 40-46, 49-55, 60-66, 68 and 70-76 will be pending in this application. Claim 26 is amended to depend from claim 25 rather than claim 1. Claims 29-31 and 49-51 are amended to recite that the recited perfusion is performed at certain times after removal of blood. Support for the amendment to these claims is found at page 5, last paragraph. Claim 37 is amended to delete the term "$CD34^+$." Claims 70-72 are substantially re-presentations of canceled claims 37-39, respectively. Claims 40 and 41 are amended to replace "contains" with "comprises." Claims 73-77 are substantially re-presentations of canceled claims 47 and 56-59, respectively. Support for these amendments and additional claims can be found in the application as originally filed and in the claims as originally filed.

It is submitted that no new matter has been introduced by the present amendments and new claims and entry of the same is respectfully requested. By the amendments and cancellation, Applicant does not acquiesce to the propriety of any of the Examiner's rejections and does not disclaim any subject matter to which Applicant is entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (1997). Further, Applicant reserves the right to prosecute the subject matter of any canceled claim in one or more continuation, continuation-in-part, or divisional applications.

Claim Objections

The Examiner has objected to claims 37-39 as having been amended but identified as "previously added." Claims 37-39 have been canceled, and have been substantially re-presented as claims 70-72.

The Examiner also objects to claims 47 and 56-59 as having been identified as "new," but containing marks of amendment. Claims 47 and 56-59 have been canceled, and have been substantially re-presented as new claims 73-77, respectively, without marks of amendment.

The Rejection Under 35 U.S.C. § 112, ¶ 1 Should Be Withdrawn

The Examiner newly rejects claims 1, 25-27 and 29-69 under 35 U.S.C. § 112, ¶ 1, as allegedly non-enabled. Office Action at pages 3-5.[1] Applicants traverse because the Examiner has not made out a case of non-enablement under the applicable legal standards.

Analysis of enablement requires a determination of whether the "disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention." MPEP 2164.01 at page 2100-178. One skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention. *See Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990). The standard for determining whether a claim is enabled or not is whether it requires undue experimentation to practice. *Id.*; *see also Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916); *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). In *Wands*, the Federal Circuit outlined several non-exclusive factors to consider in a determination of whether claims were enabled, including: A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In *Wands*, the Federal Circuit held that a particular method requiring substantial experimentation was nonetheless enabled, because the experimentation was routine.

In making the rejection, the Examiner does not explain how the disclosure fails to enable the full *scope* of the claims (indeed, the Examiner does not explain what the Examiner perceives the scope of the claims to be), the quantity of experimentation that would ostensibly be required to practice the claimed invention, or how practice of the claimed the method would require *undue* experimentation by a person of skill in the art.

To support the rejection of the claims for non-enablement, the Examiner states:

> [T]he specification fails to disclose any data that illustrates the functional characteristics of isolated cells, e.g. what kind of surface

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[1] Applicant notes that this is the first time the Examiner has found claims in this application nonenabled, despite having twice previously examining substantially similar claims. Applicant further points out that the Examiner did not raise enablement as a potential issue when amendment of the claims was discussed in the Interview of March 9, 2004. The Examiner is required to avoid piecemeal examination. *See* 37 C.F.R. 1.104(b) ("The examiner's action shall be complete as to all matters . . ."); *see* also Manual of Patent Examining Procedure ("MPEP") 707.07(g).

> markers they bear, whether they are terminally differentiated, monopetent [*sic*, monopotent] progenitor cells, or multipotent or totipotent stem cells. Although it is known in the art that the cord blood cells comprise multipotent cell, it is unknown and the specification fails to disclose that the residual cells from the extra-vascular space of a placenta contain multipotent stem cells, and they differ [*sic*] from cells collected from the extra-vascular space of any connective tissue.

Office Action at page 4.

This assertion of nonenablement is insufficient in several respects. First, the specification does, indeed, disclose that stem cells may be derived from the placenta. For example, page 12 clearly states that at least one population of cells collected from the placenta had characteristics very similar to bone marrow-derived MSC (*i.e.*, mesenchymal *stem* cells). Second, the assertion does not take into account that placental perfusion is, in certain respects, a well-developed art (*see, e.g.*, the art cited in the previous Office Action; *see also* Myllynen, "In Search of Models for Hepatic and Placental Pharmacokinetics," dissertation, University of Oulu (2003), a copy of which is attached hereto, and references cited therein), as are certain technologies related to the collection of cells from liquid suspensions and the identification of stem cells.

Moreover, what is claimed is a *method*, and the steps of that method are certainly enabled. When a person of skill in the art perfuses the recited bloodless placenta according to the method of independent claims 1 and 25, that person necessarily collects stem cells. The specific characteristics of the stem cells collected is irrelevant as long as the stem cells are necessarily obtained when one follows the claimed method. The characteristics of various stem cells were also well-known at the time of filing (*see, e.g.*, van Bekkum, *Verh. Dtsch. Ges. Pathol.* 74:19-24 (1990); Caplan, *Clin. Plast. Surg.* 21(3):429-435 (1994)).

The method as claimed in claim 1, in particular, is not limited to a particular *type* of stem cell, only the stem cells' source. Except for surface marker CD34, recited in claim 25 and claims depending therefrom, the claims do not require particular surface markers, nor do the claims differentiate between monopotent, multipotent or totipotent stem cells. Of course, stem cells cannot, as the Examiner appears to suggest, be terminally differentiated. In any event, the identification and characteristics of stem cells, generally, was well-known in the art at the time of filing (*id.*), and need not have been described in the specification.

The Examiner states that the "claims are drawn to a novel method of obtaining residual stem cells within the parenchyma and extra-vascular space of a placenta," and that "the

specification fails to disclose that the residual cells from the extra-vascular space of a placenta contain multipotent stem cells . . ." Office Action at page 4. However, none of the claims, either pending or as amended, recites the term "extravascular space" or requires that the recited stem cells originate in a particular part of the placenta.[2] As such, it appears that the Examiner is reading a limitation into the claim, and faulting the specification for not including that limitation. Applicants, in the Interview of March 9, 2004, and in the previous Amendment filed April 13, 2004, explained the *hypothesis* that stem cells migrate during culture from the placental extravascular space into the intravascular space, facilitating collection by perfusion. However, this was simply to illustrate the claimed method. Applicants are not required to explain *why* an invention works, only to teach how to make and use it. That is, the specification need not explain that the perivascular space of the placenta contains stem cells to enable one of skill in the art to collect those cells. Rather, the specification need only teach, as it does, removal of blood and perfusion at particular times to collect the cells. This statement by the Examiner, therefore, does not serve as a basis for an enablement rejection.

The Examiner further states that it is not clear whether the recited stem cells "differ from cells collected from the extra-vascular space of any connective tissue." Office Action at page 4. It is unclear to Applicants how this statement serves as a basis for a non-enablement rejection, as it does not explain how the description correlates with the scope of the subject claims, or how much (or little) experimentation is required by a person of skill in the art to practice the invention as claimed, or why such experimentation would be undue. Applicants submit that this statement by the Examiner is not a legally sufficient basis for a nonenablement rejection.

In fact, the claimed method is enabled because the specification teaches how to obtain a placenta, how to remove the placental blood, how to culture the placenta, and how to perfuse the placenta so as to collect cells. Each of these steps is straightforward and, when performed according to the specification, necessarily results in the collection of stem cells. Applicants therefore respectfully request that the Examiner withdraw the rejection of claims 1, 25-27 and 29-69 on this basis.

The Examiner has also rejected claims 26, 27, 47 and 48 under 35 U.S.C. § 112, first paragraph, as allegedly nonenabled. In particular, the Examiner asserts that the specification fails to teach how $CD34^+$ cells may be separated from $CD34^-$ cells by centrifugation. Applicants have canceled claims 26, 27, 47 and 48, thus mooting the Examiner's rejection of

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[2] Of course, the claims *do* require that the stem cells be derived from the placenta, and not from the placental or cord *blood*.

these claims on this basis. Applicants have canceled these claims without prejudice, and reserve the right to prosecute these claims in this or a related application. Applicants have canceled claims 26, 27, 47 and 48 solely to further prosecution and allowance of the remaining claims, and not as a concession the rejection for nonenablement is correct.

Cancellation of these claims notwithstanding, and with respect to the Examiner's specific basis of rejection, Applicants believe the enablement rejection of claims 26, 27, 47 and 48 to be legally insufficient. In particular, the Examiner does not explain what experimentation would be necessary to teach what the Examiner believes the specification does not teach, and how a person of skill in the art would have to practice undue experimentation in order to separate $CD34^+$ cells from $CD34^-$ cells.

Moreover, in focusing on centrifugation, the Examiner appears to argue that disclosure of centrifugation to separate $CD34^+$ cells from $CD34^-$ cells is necessary to enable these claims. However, it has never been the law of enablement that all embodiments, or even more than one embodiment, are required to enable a claim. With respect to claims 26 and 47, Applicants, as the Examiner has pointed out, have described one embodiment for separating these two cell types (*i.e.*, fluorescence-activated cell sorting). This basis of nonenablement is therefore clearly insufficient for these claims. With respect to claims 27 and 48, Applicants point out that the specification need not teach what is already well-known in the art. At the time the specification was filed, the use of centrifugation to separate cells on the basis of different markers, for example, by antibody-coated magnetic beads, was already well-known. As such, a person of skill in the art would have had to exercise only *routine* skill to practice the invention as embodied in claims 26, 27, 47 and 48.

Finally, the Examiner has rejected claim 67 under 35 U.S.C. § 112, first paragraph as allegedly nonenabled. Applicants have canceled claim 67, thus mooting the Examiner's rejection of this claim on this basis. Applicants cancel claim 67 without prejudice, and solely to further prosecution of the remaining claims, and reserve the right to prosecute this claim in this or a related application.

The Rejection under 35 U.S.C. § 112, ¶ 2 Should be Withdrawn

The Examiner rejects claims 1, 25-27, 36, 37 and 69 under 35 U.S.C. § 112, ¶ 2 as allegedly indefinite. Office Action at page 6. Applicants traverse as follows.

The Examiner states that claim 69 is indefinite in its recitation of "embryonic-like" stem cells because "the specification fails to define what type of cells are considered as 'embryonic-like stem cells.'" Office Action at page 6. Applicants disagree with the Examiner's characterization of the specification, and do not concede that the term is

insufficiently defined. However, because at least independent claim 1 encompasses the subject matter of claim 69, Applicants hereby cancel claim 69 without prejudice, reserving the right to prosecute this claim in this or a related application.

The Examiner also states that claims 26, 36 and 37 are indefinite in their recitation of "said $CD34^+$ stem cells," because this term allegedly lacks antecedent basis. Applicants have amended claim 26 to depend from claim 25 rather than claim 1; "said $CD34^+$ stem cells" in claim 26 as amended has the appropriate antecedent basis, as does claim 27, which depends from claim 26. Applicants have also amended claims 36 and 37, ultimately dependent from claim 1, to delete the term "$CD34^+$," which is lacking in claim 1. Claims 36 and 37 now have the appropriate antecedent basis for all dependent limitations.

The Examiner has not, however, explained how claims 1 and 25 are indefinite, and the grounds of indefiniteness stated by the Examiner for claim 69, and for claims 26, 36 and 37, are not applicable to claims 1 and 25. Applicants request that the Examiner withdraw the rejection of claims 1 and 25 on this basis.

The Nonstatutory Double Patenting Rejection Should Be Withdrawn

The Examiner has provisionally rejected claim 1 of the instant application over claim 16 and 17 of co-pending United States Patent Application No. 10/074,976 ("the '976 application"). Office Action at page 6. Applicants stipulate that, on June 22, 2004, Applicants, in a Response to Restriction Requirement issued by Examiner Deborah Crouch, elected a group of claims for examination that did not include claim 16 and 17. Thus, in the '976 application, claims 16 and 17 are no longer in active prosecution, and pose no potential double patenting issue. Applicants request that the provisional rejection of claim 1 on this ground be withdrawn.

CONCLUSION

Applicant respectfully requests that the above remarks and accompanying documents be entered in the present application file. An early allowance of the present application is respectfully requested.

No fee is believed due for this Amendment. However, if a fee is due, please charge such fee to Jones Day Deposit Account No. 503013.

Respectfully submitted,

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